Effects of Anisotropic Optical Parameters on the Penetration of Photons in Turbid Media

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Abstract

There are by now many applications of methods based on near-infrared radiation (NIR) used for optical imaging and therapeutic purposes in medical contexts. Such optical techniques are appealing in not requiring potentially harmful ionizing radiation and in being non-invasive. Since photons are randomly scattered by components of cells successful use of NIR requires knowledge of statistical properties of photon trajectories. Very often the requisite analysis is based on diffusion theory and the assumption of isotropic optical parameters. As one parameter characterizing a trajectory there is the local time, or amount of time spent by a photon at a specific plane interior to the turbid medium, given it is detected on the top planar surface at a time τ. The present analysis is based on a continuous-time random walk formalism, and both gated time and continuous wave experiments are analyzed and approximate analytical formulas derived.
Keywords: optical imaging, lattice random walk, continuous-time random walk, transport-corrected scattering coefficient, local time

1. Introduction

Light in all of its manifestations is universal in life as we know it. What is perhaps less well known is that the use of light as a means of biomedical imaging was suggested in a morbidity report as long ago as early nineteenth century as a means for detecting breast tumors, although it was never put to a real test in that era, [1]. A more recent experimental test of this notion was put forth by Cutler, [2], in 1929 with no real success because the scientific infrastructure for its successful implementation was hardly available. It was only within the last thirty years that the availability of lasers and sophisticated computing technology has permitted the development and exploitation of an enormous number of optically-based techniques in biomedical settings, both for imaging and therapeutic purposes.

Typically, in optical imaging measurements, photons that are injected by means of a laser into a tissue to be examined, are scattered by various inhomogeneities within the tissue, and then may be re-emitted through a boundary surface where they are detectable as light intensity. This intensity is the source from which information can be deduced which may be related to the state of underlying tissue. The use of optical methods in the near-infrared spectrum is attractive because it is non-invasive and, as far as is known, non-carcinogenic [3]. However, since photons are randomly scattered by heterogeneities found in cells, and it is necessary to know which part of the anatomy has been interrogated by the photons, it is necessary to analyze photon paths by means of some form of transport theory to characterize photon trajectories in some format or other. In its most general form this requires considerable numerical calculation, and a knowledge of physical properties of the scattering bodies is not easy to obtain experimentally. Very often, a straightforward form of diffusion or random walk theory provides the theory since the types of geometries dealt with are often relatively simple, e.g., it is often adequate to assume the tissue to be an infinite slab or a semi-infinite bulk medium. However, when the optical parameters that characterize the underlying tissue are anisotropic with respect to surfaces that separate the tissue from the exterior the mathematical analysis can be more complicated. The presence of anisotropic optical properties sometimes requires somewhat intricate methods to provide the intermediate steps of translating experimental data into biophysically usable information.

Since transport phenomena essentially implies randomness, the language and techniques of probability theory provide a natural framework for describing photon motion in a turbid medium. There are obviously many ways to do this. One technique used in diverse statistical physics investigations is based on the notion of residence times, i.e., the fraction of time that a diffusing particle spends in a specified planar region of the turbid medium relative to the total time. In the present note we extend an analysis originally developed in the framework of the formulation of photon diffusion in turbid media as a lattice random walk, [4, 5], for the case in which optical properties of the medium were all taken to be isotropic. The residence time spent at a given distance from a planar interface conditioned on the photon leaving that surface at a specified time and position was first proposed as a parameter characterizing photon trajectories in the context of biomedical optics in [6]. Its application along these lines was later extended in [7] and [8]. We propose to now extend some of the methods used to incorporate effects of anisotropy.

Notice that it would be somewhat awkward to carry out such a program starting from a purely diffusion formulation since, at the very least, one would have to replace a line in the present formulation, $z = Z$, by a slab centered at an arbitrary plane and having an arbitrary thickness. This approach, however, allows too many degrees of freedom to be really practical.

2. Formulation of the model

The two major assumptions in the present analysis is (i) that diffusion in the continuum can be replaced by a random walk on a simple cubic lattice and (ii) that the principal axis of the anisotropy in the turbid medium coincide with those of the lattice and that within a given plane the medium is isotropic. Each point of the lattice will be specified by $\mathbf{r} = (x, y, z)$ where x, y and z are taken to be integers whose ranges are $-\infty < x, y < \infty$ and $0 \leq z < \infty$. That is to say, we consider a semi-infinite medium bounded by a plane $z = 0$, where $z > 0$ corresponds to points within the medium. The optical parameter of greatest interest is μ_s', the transport-corrected scattering coefficient. The lattice coordinate $\mathbf{r}$ is related to the physical coordinate $\mathbf{r}_{\text{phys}}$ by $\mathbf{r}_{\text{phys}} = \mathbf{r}(\sqrt{2}/\mu_s')$ as established in two studies of scaling relations by Gandjbakhche et al, [9, 10]. The only difference now is that μ_s' is measured for the within the plane scattering.

Insofar as possible we shall try to obtain results in closed form. For this purpose we restrict ourselves to nearest-neighbor random walks, which is to say that a photon at (x, y, z) will be allowed, at any step, to move to only one of the sites $(x \pm 1, y \pm 1, z \pm 1)$. The choice of the particular site to which the step will be made is determined by the anisotropy, as defined below. The starting point of any analysis must obviously be based on the propagator. A most convenient way to proceed in the present problem is to use the continuous-time random walk (CTRW), [11, 12]. In the CTRW the time between successive steps is taken to be a random variable. Considerable simplification results if the probability density for this random time, $\psi(t)$, is chosen to have the form

$$\psi(t) = ke^{-kt} = e^{-\tau} \tag{1}$$

in which $k = c\mu_s'$ is a rate constant, and c is the speed of light in the tissue, so that τ is a dimensionless time.

A second assumption is needed to define the anisotropy. Note that the anisotropy could have been modeled by using a non-uniform lattice, however, here we treat μ_s' and the rate constant k for the successive steps as isotropic, but the probabilities that such a jump occurs along a specific axis are not. Let the probability that the photon makes a single step along the x axis ($x \to x \pm 1$) be α, $y \to y \pm 1$ be β and $z \to z \pm 1$ be γ so that $2\alpha + 2\beta + 2\gamma = 1$. Isotropy is therefore equivalent to the choice $\alpha = \beta = \gamma = 1/6$. Here we will assume that $\alpha = \beta$. The initial position of the photon is taken to be $\mathbf{r}_0 = (0, 0, 1)$. In the absence of boundaries, the propagator can be shown to be, [15],

$$p^{(F)}(\mathbf{r}; \tau|\mathbf{r}_0) = e^{-\tau} I_x(2\alpha\tau) I_y(2\beta\tau) I_{z-1}(2\gamma\tau) \tag{2}$$

where the $I_m(u)$ are modified Bessel functions of the first kind, [14]. At sufficiently long times $p^{(F)}(\mathbf{r}; \tau|\mathbf{r}_0)$ approaches a Gaussian limit which is what one expects on the consideration that one is dealing with a random walk for which the central limit holds. Equation (2) is only an intermediate result since it holds only in free space. What is needed is an expression for the propagator that vanishes on the plane $z = 0$. Since the x and y components of the free-space propagator appear in a factored form, and $\mathbf{r}_0 = (0, 0, 1)$, the propagator that satisfies the boundary condition $p(x, y, 0; \tau|\mathbf{r}_0) = 0$ can be shown to be, [15],

$$p(\mathbf{r}; \tau|\mathbf{r}_0) = ze^{-\tau} I_x(2\alpha\tau) I_y(2\beta\tau) I_z(2\gamma\tau)/(2\gamma\tau) \tag{3}$$

which clearly vanishes at $z = 0$.

By the local time at $z = Z$ at time τ we will mean the total time spent spent on that plane by a photon emerging anywhere at the surface at time τ. This can be considered as a measure of the depth probed by photons detected at the surface at time τ. In the remainder of our analysis we derive statistical properties of the local time as a function of the parameters just defined. The utility of the formalism presented to this point is that the propagator given in Eq.(3) factors into functions of the three spatial variables, which serves to simplify the mathematical problem to a considerable extent.

3. Analysis

3.1. Time-gated experiments

There are two basic types of time-dependent experiments used in biomedical applications; time-gated measurements and continuous-wave (CW) experiments. In the first of these the optical input can be regarded as a pulse and the output is measured as a function of time while in CW measurements both the input and output are continuous signals. To find the local time in both cases requires a knowledge of the time-dependent propagator. We therefore begin by studying the time-gated experiment.

Let the time at which the photon escapes at $z = 0$ be equal to τ and let two earlier times be $\tau'' < \tau'$ where, of course, $\tau' < \tau$. Denote the total time spent at $z = Z$ during the time τ, the local time, by $T_{\text{local}}(\tau|Z)$. We initiate the calculation by considering the contribution of the time interval $(\tau'', \tau''+d\tau'')$ to the local time spent at $z = Z$ as a function of both Z and τ. To examine this function it will be necessary to examine the entire trajectory from $\mathbf{r}_0$ to an arbitrary point on the surface $\mathbf{R} =(X, Y, 0)$ and lastly, sum over all possible X and Y.

A trajectory which passes through $z = Z$ can be represented schematically as

$$(0, 0, 1; 0) \to (x, y, Z; \tau'') \to (X, Y, 1; \tau') \to (X, Y, 0; \tau) \tag{4}$$

This may be interpreted as follows: At $\tau = 0$ the photon is at $(0, 0, 1)$ from which point it moves to (x, y, Z), arriving there during the time interval $(\tau'', \tau'' + d\tau'')$. The trajectory from $(0, 0, 1)$ to (x, y, Z) is described by the propagator in Eq.(3). The coordinates x and y can take on all possible values, and all are to be summed over in the course of the analysis. The random walk takes place on a simple cubic lattice, and has been defined to be a nearest-neighbor random walk which terminates at $(X, Y, 0)$. Therefore its position just prior to termination must be at $(X, Y, 1)$ at some time $\tau' > \tau''$ and the time at which it reaches $z = 0$ is $\tau > \tau'$. As mentioned, the final step in the derivation consists in summing over X and Y.

The first step in analyzing the sequence in Eq.(4) requires us to sum over all

x and y using the propagator in Eq.(3). This produces a function $S_1(\tau'')$ where

$$S_1(\tau'') = \frac{Ze^{-\tau''}}{2\gamma\tau''} I_Z(2\gamma\tau'') \sum_{x=-\infty}^{\infty} \sum_{y=-\infty}^{\infty} I_x(2\alpha\tau'') I_y(2\beta\tau'') \tag{5}$$

The values of the two sums can be derived from the general formula, [14],

$$\sum_{x=-\infty}^{\infty} I_x(m) = e^m \tag{6}$$

together with the exponents $\tau''(-1+2\alpha+2\beta) = -2\gamma\tau''$, so that Eq.(5) reduces to a function of two variables, Z and $2\gamma\tau''$ which we denote by $U_Z(2\gamma\tau'')$:

$$U_Z(2\gamma\tau'') = \frac{Ze^{-2\gamma\tau''}}{2\gamma\tau''} I_Z(2\gamma\tau'') \tag{7}$$

The next step in dealing with the sequence in Eq.(4) requires considering the subsequence $(x, y, Z; \tau'') \to (X, Y, 1; \tau')$. To this end we can simply appeal to an argument based on symmetry to derive the contribution from this component, to infer that it is basically the same as $S_1(\tau'')$ except that now the time τ'' that appears in Eq.(5) or (7) is to be replaced by $(\tau'-\tau'')$. Hence, the second component takes a form similar to that in Eq.(7) and yields:

$$S_2(\tau' - \tau'') = U_Z[2\gamma(\tau' - \tau'')] \tag{8}$$

Lastly, the final step takes the random walk from $(X, Y, 1)$ to $(X, Y, 0)$. The probability density for this event is equal to $\gamma e^{-\gamma(\tau-\tau')}$.

Having now assembled the separate components of the trajectory, we can calculate $T_{\mathrm{local}}(\tau|Z)$ in terms of convolution integrals and write

$$T_{\mathrm{local}}(\tau|Z) = \gamma \int_0^{\tau} e^{-\gamma(\tau-\tau')} d\tau' \int_0^{\tau'} U_Z(\tau'') U_Z[(\tau' - \tau'')] d\tau'' \tag{9}$$

While this appears somewhat complicated, an equivalent and simpler looking expression is available in terms of Laplace transforms. This has the further advantage that it leads directly to the comparable solution for the CW case. Let $\hat{h}(s)$ denote the transform of a generic function of time $h(t)$. Using this notation on Eq.(9) one finds

$$\hat{T}_{\mathrm{local}}(s|Z) = \frac{\gamma}{s+\gamma} \hat{U}_Z^2(s) \tag{10}$$

The transform of Eq.(7) or (8) can be found from standard tables to be, [16],

$$\hat{U}_Z^2(s) = \frac{1}{2\gamma}\left[\frac{2\gamma}{s+2\gamma+\sqrt{s^2+4\gamma s}}\right]^Z \tag{11}$$

We have not been able to invert this in closed form, but it can be inverted numerically. The long-time behavior of $T_{\mathrm{local}}(\tau|Z)$ can be determined by passing to the $s \to 0$ limit of the expression in square brackets, which yields an approximation to $\hat{U}_Z^2(s)$ as

$$\hat{U}_Z^2(s) \approx \frac{1}{2\gamma}\left(1+\sqrt{\frac{s}{\gamma}}\right)^{-Z} \tag{12}$$

By taking logarithms of this relation and retaining the lowest order in s we find

$$\ln\left[\hat{U}_Z^2(s)\right] \approx \ln\left(\frac{1}{2\gamma}\right) - Z\ln\left(1+\sqrt{\frac{s}{\gamma}}\right) \approx \ln\left(\frac{1}{2\gamma}\right) - Z\sqrt{\frac{s}{\gamma}} \tag{13}$$

or

$$\hat{U}_Z^2(s) \approx \frac{1}{2\gamma}\exp\left(-Z\sqrt{\frac{s}{\gamma}}\right) \tag{14}$$

An inversion of this transform, together with Eq.(10) leads to an approximation which we expect to be valid at long times

$$T_{\mathrm{local}}(\tau|Z) \approx \frac{Z}{4\sqrt{\pi(\gamma\tau)^3}}\exp\left(-\frac{Z^2}{4\gamma\tau}\right) \tag{15}$$

which is seen to have a single maximum as a function of Z at $Z_{\max} = (2\gamma\tau)^{1/2}$. It should be noted that the term $\gamma/(s+\gamma)$ that appears in Eq.(10) is equal to unity for small s in comparison to that in Eq.(12) and therefore can be neglected in the long-time limit.

Figure 1 compares the numerical Laplace inversion of Eq.(11) with the approximation in Eq.(15) for $\gamma = 0.1, 0.3$ and $Z = 1, 3, 10$, where the results are plotted for different ranges of τ values. For large τ, $T_{\mathrm{local}}(\tau|Z)$ goes asymptotically to zero as $\tau^{-3/2}$, a power-law behavior predicted by the formula in Eq.(15), and which agrees with the numerically exact result. For $Z > 1$ the approximation approaches the exact results quickly and for $Z > 10$ the approximation and the exact result are virtually indistinguishable for any value of τ. Further extensions of the present analysis that might be of some physical interest involve finding properties of the local time on an arbitrary set of points, but we have not explored any of the difficulties that might have to be overcome to complete such an undertaking.

3.2. CW experiments

A solution to the time-gated problem is obviously needed to solve the analogous problem for CW experiments. The relation between the two solutions is direct. Let $g(\tau)$ be the probability density for a photon lifetime within the bulk, that is, the time between the photon injection and the time that it leaves the medium, and let $[T_{\rm local}(Z)]_{CW}$ be the local time in a CW experiment. This function is related to $T_{\rm local}(\tau|Z)$ by

$$[T_{\rm local}(Z)]_{CW} = \int_0^\infty T_{\rm local}(\tau|Z)g(\tau)d\tau \tag{16}$$

leaving us only with the problem of calculating $g(\tau)$. This can be done by analyzing the trajectory

$$(0,0,1;0) \to (X,Y,1;\tau') \to (X,Y,0;\tau) \tag{17}$$

which is similar to Eq.(4) without the term $(x,y,Z;\tau'')$. An analysis following that in the preceding subsection leads to the expression

$$g(\tau) = \frac{1}{2}\int_0^\tau e^{-2\gamma\tau'}\frac{I_1(2\gamma\tau')}{\tau'}e^{-\gamma(\tau-\tau')}d\tau' \tag{18}$$

While this integral cannot be evaluated exactly its Laplace transform is found to be, [16],

$$\hat{g}(s) = \frac{s+2\gamma-\sqrt{s^2+4\gamma s}}{4\gamma(s+\gamma)} = \frac{\gamma}{(s+\gamma)\left[s+2\gamma+\sqrt{s^2+4\gamma s}\right]} \tag{19}$$

It is again possible to find $g(\tau)$ from its transform by numerically inverting it. A long time approximation to $g(\tau)$ can be determined by passing to the limit $s \to 0$, leading to the somewhat simplified transform

$$\hat{g}(s) \approx \frac{\sqrt{\gamma}}{2(s+\gamma)\left(\sqrt{s}+\sqrt{\gamma}\right)} \tag{20}$$

The calculation of $\hat{g}(s)$ in the $s \to 0$ follows that in the preceding section except that the factor Z that appears there is to be replaced by 1. Consequently, an approximate form for the long-time limit of $g(\tau)$ is

$$g(\tau) \approx \frac{1}{4\sqrt{\pi(\gamma\tau)^3}}\exp\left(-\frac{1}{4\gamma\tau}\right) \tag{21}$$

which decays as $\tau^{-3/2}$. Since $g(\tau)$ is equivalent to $T_{\mathrm{local}}(\tau|Z=1)$ one can see in the top row of Figure 1 (Z=1) that this approximation works well only at large values of τ. Nevertheless, using Eqs. 15 and 21 we can arrive at approximate analytic expression for $[T_{\mathrm{local}}(Z)]_{CW}$, i.e.,

$$[T_{\mathrm{local}}(Z)]_{CW} = \frac{Z}{\pi\left(Z^2+1\right)^2\gamma} \tag{22}$$

In Figure 2 we compare this expression with the accurate result obtained by numerical Laplace inversion and integration. Figure 2(a) plots the approximate and exact results*versus* Z for $\gamma = 0.1$. As Eq.(22) indicates, the approximation depends on γ only as the scale factor, while the ratio of the approximate and the exact results varies only slightly as a function of γ (see Figure 2(b)). As Z increases the approximation in Eq.(22) approaches the exact result, as can be seen in Figures 2(a) and 2(b).

4. Conclusions

Optical techniques for biomedical imaging are becoming increasingly popular because they require no potentially dangerous ionizing radiation and optical techniques based on photons when used in the near-infrared (roughly between 400 and 1100 nm) are potentially sensitive to metabolic processes and blood flow. However, a drawback is that photons are also scattered in that range of wave lengths. Consequently, the problem of establishing the properties of the volume interrogated by photon trajectories in biological tissues is an important one. In view of the fact that many tissues are now known to have anisotropic optical properties it is worthwhile the effects of this possibility.

In the present note we have worked with a model in which the diffusion is represented by a CTRW on a simple cubic lattice in which the anisotropy corresponds to differences in transition probabilities for movement along different axes of the lattice. This model was first suggested and partially analyzed in [17]. The random variable under investigation in the present note is the so-called local time. That is, if a photon is injected into tissue and later emerges from the tissue after a (dimensionless) time τ we ask for the local time or total amount of time spent at a depth Z out of the total travel time. A complete solution for the local time in both time-gated and continuous wave measurements is given in terms of Laplace transforms. The asymptotic ($\tau \to \infty$) solution is shown to have a single maximum as a function of Z and is proportional to $\tau^{-3/2}$ in the case of time-gating and has a single maximum as a function of Z in the case of continuous-wave measurements.

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References

[1] R. Bright, vol. 2, Longman, London (1831) 431.

[2] M. Cutler, Surg. Gynec. Obstet. 48 (1929) 721.

[3] D.A. Benaron, W. Cheong and D.K. Stevenson, Science 276 (1997) 2002.

[4] R.F. Bonner, R. Nossal, S. Havlin and G.H. Weiss, J. Opt. Soc. A 4 (1987) 1987 423.

[5] A.H. Gandjbakhche and G.H. Weiss, in Progress in Optics, E. Wolf (ed.) vol. XXXIV 1995 333.

[6] G.H. Weiss, R. Nossal and R.F. Bonner, J. Mod. Opt. 36 (1989) 349.

[7] G.H. Weiss, Appl. Opt. 37 (1998) 3558.

[8] G.H. Weiss, J.M. Porrà and J. Masoliver, Phys. Rev. E (1998) 6431.

[9] A.H. Gandjbakhche, R.F. Bonner and R. Nossal, J. Stat. Phys. 69 (1992) 35.

[10] A.H. Gandjbakhche, R. Nossal and R.F. Bonner, Med. Phys. 32 (1993) 504.

[11] G.H. Weiss, Aspects and Applications of the Random walk, North-Holland, Amsterdam, 1994.

[12] B.D. Hughes, Random Walks and Random Environments, Vol. 1: Random Walks, Clarendon Press, Oxford, 1995.

[13] D.J. Bicout and G.H. Weiss, Opt. Comm. 158 (1998) 213.

[14] M. Abramowitz and I.A. Stegun (eds.), Handbook of Mathematical Functions, Dover, New York, 1972.

[15] G.H. Weiss, J.M. Porrà and J. Masoliver, Opt. Comm. 146 (1998) 268.

[16] G.E. Roberts and H. Kaufman, Table of Laplace Transforms, W.B. Saunders, Philadelphia, 1966.

[17] L. Dagdug, G.H. Weiss and A.H. Gandjbakhche, Phys. Med. Biol. 48 (2003) 1361.

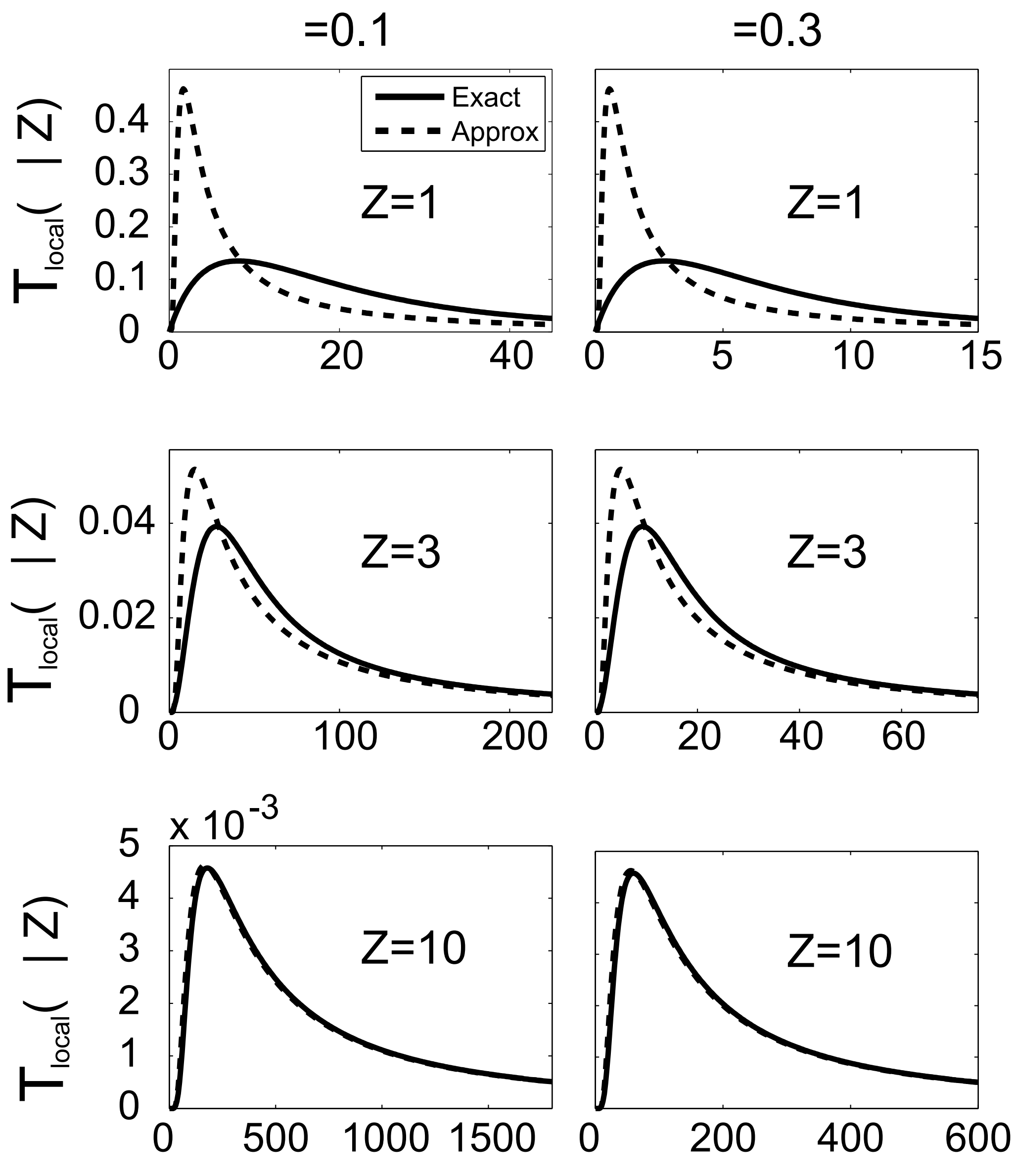

Figure 1: Plot of $T_{\text{local}}(\tau|Z)$, comparing the numerical Laplace inversion of Eq.(11) with the approximation in Eq.(15), for $\gamma = 0.1$ (left column) and $\gamma = 0.3$ (right column), and for three values of $Z = 1, 3, 10$, as indicated on each figure. For $\gamma = 0.1$ (0.3) anisotropy is such that the photons are more (less) likely to remain in the plane than in the isotropic tissue ($\gamma = 1/6$).

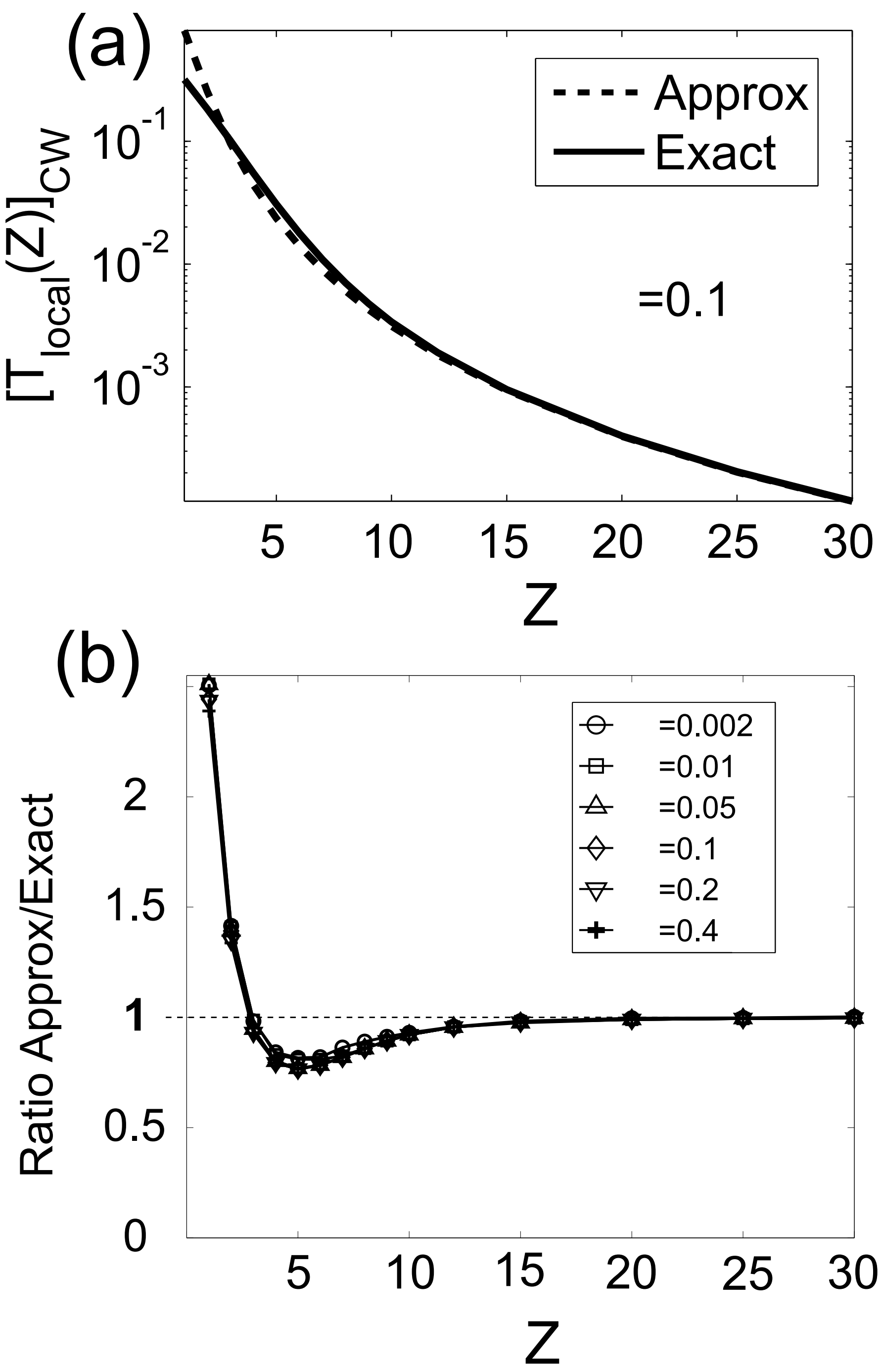

Figure 2: (a) Plot of $[T_{\mathrm{local}}(Z)]_{CW}$, comparing the approximate result in Eq.(22) to exact numeric evaluation for $\gamma = 0.1$. The results are plotted on semi-logarithmic plot to emphasize the agreement at larger values of Z. (b) Plot of the ratio of the approximate result and the exact numeric result as a function of Z, for six different values of $\gamma = 0.002, 0.01, 0.05, 0.1, 0.2, 0.4$.